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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/536,860	01/06/2006	Hana Golding	65831 (47992)	4611

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EXAMINER	
CHEN, STACY BROWN	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
01/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,860	GOLDING, HANA	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7,12-15,17,18 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,12-15,17,18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendment filed October 20, 2008 is acknowledged and entered. Claims 1, 5, 7, 12-15, 17, 18 and 21 are pending and under examination.

Claims Summary

2. The claims are drawn to a method of determining whether a candidate agent modulates invasion of a cell by a labeled virus, specifically vaccinia. The method comprises incubating a mixture of at least one cell, a labeled virus that encodes a detectable label, and a candidate agent. A decrease of detection of the label within the cell indicates that the candidate agent decreases invasion of the cell by the virus. Specifically, the candidate agent decreases invasion of the cell by the labeled invasin. The detectable label is a fluorescent protein or enzyme. The candidate agent is a monoclonal, a polyclonal or altered antibody. An altered antibody includes antibody fragments described on page 11, lines 13-16. The antibody associates with the labeled invasin. The Office interprets "associates with" to be equivalent to the antibody binding the invasin. Specifically, the cell is a mammalian cell, such as a human cell (lymphoid, pulmonary or intestinal).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 7, 12-15 and 17 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Domínguez *et al.* (*Journal of Immunological Methods*, 1998, 220:115-221,

"Domínguez") in view of Hooper *et al.* (US Patent 6,451,309, "Hooper"). The claims are summarized above. Domínguez discloses green fluorescent protein (GFP) expressed by a recombinant vaccinia virus that permits early detection of infected cells by flow cytometry (abstract). Domínguez uses the construct as an infection tag and teaches that it is useful for studying tropism in a complex cell population such as porcine PBMCs (page 116, first column, third full paragraph). Domínguez does not disclose the use of the construct for testing the anti-viral activity of candidate agents, particularly antibodies.

However, Hooper teaches the production and identification of vaccinia monoclonal antibodies for the purpose of therapeutic treatment (passive immunization) of vaccinia in humans (abstract). Hooper discloses that potential targets for poxvirus therapeutics, monoclonal antibodies, were generated in mice and tested for their ability to neutralize virus and protect mice from challenge (col. 2, lines 5-20). Hooper teaches that the neutralizing activity of the antibodies was not always predictive of protective efficacy in mice upon challenge.

It would have been obvious to use the vaccinia-GFP construct of Domínguez to test the infectivity of cells in the presence of Hooper's monoclonal antibodies to determine whether the antibodies are effective agents that inhibit vaccinia virus infectivity (*i.e.*, decrease of viral entry as a result of binding with the monoclonal antibody). One would have been motivated to use the vaccinia-GFP construct because it shows infectivity, not merely neutralization. As is taught by Hooper, neutralization tests were not always predictive of protective efficacy in mice upon challenge (Hooper, col. 2, lines 14-20). One of ordinary skill in the art would have been motivated to use a method that better reflects the inhibiting activities of the monoclonal antibodies (decrease of viral entry as a result of binding with the monoclonal antibody), such as

the method described by Domínguez. One would have had a reasonable expectation of success because Domínguez uses a vaccinia construct, and Hooper is testing vaccinia antibodies. One would expect that, in the screening process, Hooper's antibodies (those that are capable of inhibiting vaccinia infection) would bind to the vaccinia-GFP construct of Domínguez (associate with the labeled invasin) and decrease invasion of the cell.

With regard to the limitation of claim 13 which requires that the detectable label be an enzyme, Domínguez discloses that a number of marker genes have been inserted in the vaccinia virus genome, and that their utility has been demonstrated in different experimental situations (thymidine kinase, guanine phosphoribosyl transferase, beta-galactosidase, etc.), see Domínguez, pages 115-116, bridging paragraph. Although Domínguez opts to use GFP, it is clear that enzyme labels are well known in the art to be useful in vaccinia infectivity assays. It would have been well within the ability of the ordinary artisan to elect whether to use GFP or an enzyme label depending on the circumstances of the assay. Therefore, the invention would have been obvious to one of ordinary skill in the art at the time of the invention.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that no combination of the references teaches a method to measure protection of cells by virus invasion by measuring a decrease in invasion by a candidate agent.
  - In response, it would have been obvious to use the labeled construct of Domínguez to test the infectivity of cells in the presence of Hooper's monoclonal antibodies to determine whether the antibodies are effective agents that inhibit vaccinia virus

infectivity (*i.e.*, decrease of viral entry as a result of binding with the monoclonal antibody).

- Applicant also argues that the claimed method is the only validated alternative method to the classical labor intensive plaque reduction assay. Applicant points out that high throughput technology makes the claimed method highly sensitive, easier to conduct, faster and easy to transfer to other laboratories.
  - In response, any recognized advantages of the claimed method do not render the method unobvious if the method steps are taught by the prior art, whether in an anticipation or obviousness rejection. As outlined above, the combined teachings of Domínguez and Hooper result in the claimed invention.
  - In response to applicant's argument that the Domínguez reference does not teach the use of monoclonal antibodies (candidate agents), the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

4. Claims 18 and 21 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Domínguez *et al.* (*Journal of Immunological Methods*, 1998, 220:115-221, "Domínguez") in view of Hooper *et al.* (US Patent 6,451,309, "Hooper") as applied to claims 1 and 17 above, and further in view of Engelmayer *et al.* (*The Journal of Immunology*, 1999, 163:6762-6768,

"Engelmayer"). Applicant's arguments regarding this rejection have been addressed above. The rejection is maintained for reasons of record.

Conclusion

5. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B Chen/
Primary Examiner, Art Unit 1648